UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/558,543	10/23/2006	Xiaozhu Duan	DEX0489US.NP	6173

32800 7590 07/16/2008

LICATA & TYRRELL P.C.
66 E. MAIN STREET
MARLTON, NJ 08053

EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	
NOTIFICATION DATE	**DELIVERY MODE**
07/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No.	Applicant(s)	
	10/558,543	DUAN ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,24-26,29-31,45,46,48,51 and 95-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,24-26,30,31,48 and 95-97* is/are rejected.

7)☒ Claim(s) *29,45,46 and 51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 4/14/08 in response to the Office Action of 12/14/07 are acknowledged and have been entered.

Claims 96-97 have been added by Applicant.

Claims 20, 24-26, 29-31, 45, 46, 48, 51, and 95-97 are pending.

Claims 20, 24-26, 30, 31, 45, 48, and 95 have been amended by Applicant.

Claims 20, 24-26, 29-31, 45, 46, 48, 51, and 95-97 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections necessitated by New Considerations.

Rejections Withdrawn

The rejection under 35 U.S.C. 101 is withdrawn.

The rejection under 35 U.S.C. 112, first paragraph, is withdrawn.

The rejection under 35 U.S.C. 102(b) is withdrawn.

The rejection of claims 20, 24, 26, 31, 45, 48, and 51 under 35 U.S.C. 102(e), for being anticipated by Schlegel et al (US 2003/0108693 A1; 6/12/03), is withdrawn. However, as noted below, claim 95 remains rejected under 35 U.S.C. 102(e), for being anticipated by Schlegel et al (US 2003/0108693 A1; 6/12/03).

The rejection of claims 24-25 under 35 U.S.C. 103(a), as being unpatentable over Soppet and Dillon (US 5,861,494; 1/19/99) in view of Casalini et al (Cancer Immunol Immunother, July 1993, 37:54-60), is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 95 remains rejected under 35 U.S.C. 102(e) as being anticipated by Schlegel et al (US 2003/0108963 A1; 6/12/03) for the reasons stated in the Office Action of 12/14/07 and for the reasons set-forth below.

Amended claim 95 is drawn to a kit comprising a suitable assay for measuring Cln101 levels and a suitable assay for measuring Prostate Specific Antigen (PSA) levels wherein the assay for Cln101 comprises antibodies which compete for binding to the same epitope as the epitope bound by the monoclonal antibody produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5877 and PTA-5876.

It is noted that monoclonal antibodies produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5877 and PTA-5876 specifically bind Cln101. However, the exact binding epitope(s) on Cln101 is not known.

Schlegel et al teaches a kit comprising a polyclonal antibody that binds to mammalian Cln101 as part of a kit comprising antibodies that bind PSA (see paragraphs 7, 56, 58, 113-115, and 183-184). Schlegel et al further teaches said polyclonal antibody generated by immunizing an animal with the Cln101 protein (see paragraph 184, in particular). One of skill in the art would recognize that polyclonal antibody populations contain numerous antibodies that bind numerous epitopes of the protein to which they have been generated.

Although Schlegel et al does not specifically teach polyclonal antibodies generated by Cln101 protein would compete for binding to the same epitope as the epitope bound by antibodies produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5877 and PTA-5876, cln101 antibodies of the claimed kit appear to be the same as those of the prior art, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the cln101 antibodies of the prior art do not possess the same characteristics of the cln101 antibodies of the claimed product. In the absence of evidence to the contrary, the burden is on Applicant to prove that the cln101 antibodies of the claimed product are different from that taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195

USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

In the Response filed 4/14/08, Applicant argues that claim 95 has been amended to depend from claim 30 and the claim 30 has not previously been included in this rejection.

The amendments to the claims and the arguments found in the Reply of 4/14/08 have been carefully considered, but are not deemed persuasive. In regards to the argument that claim 95 has been amended to depend from claim 30 and the claim 30 has not previously been included in this rejection, Claim 30 should have previously been rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 20 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Soppet and Dillon (US Patent 5,861,494; 1/19/99) in view of Sakamoto et al (Gut, March 1987, 28: 323-329) for the reasons stated in the Office Action of 12/14/07 and for the reasons set-forth below.

Soppet and Dillon teaches antibodies that specifically bind Cln101 would be used to detect metastatic colon cancer cells and diagnose metastatic colon cancer (see lines 31-37 of column 2, in particular).

Soppet and Dillon does not specifically teach a kit comprising a suitable assay for measuring Cln101 levels and further comprising a suitable assay for measuring CA125 levels wherein the levels of both CA125 and Cln101 are determined. However, this deficiency is made up in the teachings of Sakamoto et al.

Sakamoto et al teaches a method comprising diagnosing metastatic colon cancer by using a kit comprising an antibody that specifically binds CA125 to determine levels of CA125 in patient serum (see Table 1, in particular). Sakamoto et al further teaches that combining detection of CA125 with detection of other makers for metastatic colon cancer yielded higher sensitivities than by using a single marker (see left column of page 328, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to produce a kit comprising antibodies that bind Cln101 and antibodies that bind CA125 because Soppet and Dillon teaches a kit comprising antibodies that specifically bind Cln101 to diagnose metastatic colon cancer (see lines 31-37 of column 2, in particular), Sakamoto et al teaches a kit comprising an antibody that specifically binds CA125 to diagnose metastatic colon cancer (see Table 1, in particular), and one of skill in the art would recognize that a kit with antibodies that detect both Cln101 and CA125 would be more sensitive than a kit that detects either marker alone. One of ordinary skill in the art at the time the invention was made would have had a reasonable

expectation of success for combining the kit taught by Soppet and Dillon with the kit taught by Sakamoto because Soppet and Dillon and Sakamoto teach antibodies that specifically bind Cln101 and CA125, respectively. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

It is further noted that the kit comprising antibodies taught by the combined teachings of Soppet and Dillon and Sakamoto is a kit for diagnosing a patient's susceptibility to ovarian cancer comprising a suitable assay for measuring Cln101 levels wherein the levels of Cln101 are determined, further comprising a suitable assay for measuring CA125 levels wherein the levels of both CA125 and Cln101 are determined. It is noted that statements of intended purposes or uses are not considered limitations because they merely state an intended use of the invention rather than any distinct definition of any of the claimed invention's limitations (see Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). Thus, recitation of statements describing the claimed product as a product which is intended to diagnose a patient's susceptibility to ovarian cancer are not given patentable weight and are not limitations to the claims.

In the Reply of 4/14/08, Applicant states that page 328 discusses the false positive rates for detecting all cancers evaluated in their study (pancreatic, biliary tract, liver, colon/rectum, stomach, and esophagus), not just colon cancer. Applicant further states that when read in context, Sakamoto et al discusses results of combining markers for detection of pancreas and biliary tract cancer and not colon cancer.

Applicant concludes that the Examiner's suggested motivation to combine Sakamoto with Soppet and Dillon is unfounded. Applicant further argues that one of skill in the art would not have a reasonable expectation for success. Applicant states that colon cancers of the digestive system have different etiologies than ovarian cancer and one would not anticipate that use of markers individually in colon cancer and cancers of the digestive system would have unexpected synergistic results for detecting ovarian cancer as demonstrated in the instant application. Applicant further states that Example 5 demonstrates unexpected synergistic results for combining Cln101 and CA125 to detect ovarian cancer.

The arguments found in the Reply of 4/14/08 have been carefully considered, but are not deemed persuasive. In regards to the statement that page 328 discusses the false positive rates for detecting all cancers evaluated in their study and not just colon cancer, the following sentence spans page 327-328: "Combined tests of multiple tumour markers may provide both higher sensitivities and lower specificities than a single test, hence we must consider the increment of false positive rate in benign disease when evaluating combined tests". Sakamoto further teaches CA 125 is a marker for metastatic colorectal cancer and working examples using CA 125 combined with other markers of colorectal cancer in combined tumor marker tests for colorectal cancer (see Table 2 and page 325, in particular).

In regards to the statements that when read in context, Sakamoto et al discusses results of combining markers for detection of pancreas and biliary tract cancer and not colon cancer, Sakamoto teaches working examples using CA 125 combined with other

markers of colorectal cancer in combined tumor marker tests for colorectal cancer and teaches that CA 125 values are higher in metastatic carcinomas than in localized carcinomas (see Table 2 and page 325, in particular).

In regards to the argument that the Examiner's suggested motivation to combine Sakamoto with Soppet and Dillon is unfounded, one of ordinary skill in the art at the time the invention was made would have been motivated to produce a kit comprising antibodies that bind Cln101 and antibodies that bind CA125 because Soppet and Dillon teaches a kit comprising antibodies that specifically bind Cln101 to diagnose metastatic colon cancer (see lines 31-37 of column 2, in particular), Sakamoto et al teaches a kit comprising an antibody that specifically binds CA125 to diagnose metastatic colon cancer (see Tables 1-2 and page 325, in particular), and one of skill in the art would recognize that a kit with antibodies that detect both Cln101 and CA125 would be more sensitive than a kit that detects either marker alone.

In regards to the argument that one of skill in the art would not have a reasonable expectation for success, one of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for combining the kit taught by Soppet and Dillon with the kit taught by Sakamoto because Soppet and Dillon and Sakamoto teach antibodies that specifically bind Cln101 and CA125, respectively.

In regards to the argument that colon cancer of the digestive system have different etiologies than ovarian cancer and one would not anticipate that use of markers individually in colon cancer and cancers of the digestive system would have unexpected synergistic results for detecting ovarian cancer as demonstrated in the

instant application and that Example 5 demonstrates unexpected synergistic results for combining Cln101 and CA125 to detect ovarian cancer, an intended use for detecting ovarian cancer is not a limitation to the claim. Further, Example 5 does not demonstrate unexpected or synergistic results of kits comprising Cln101 and CA125 antibodies. As expected, both Cln101 and CA125 antibodies of the kit in Example 5 specifically bind Cln101 or CA125, respectively.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 24-26, 30, 31, 48, 96, and 97 are rejected under 35 U.S.C. 102(b) as being anticipated by Soppet and Dillon (US Patent 5,861,494; 1/19/99).

The claims are drawn to antibodies which compete for binding to the same epitope as the epitope bound by the monoclonal antibody produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5877 and PTA-5876.

It is noted that monoclonal antibodies produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5877 and PTA-5876 specifically bind Cln101. However, the exact binding epitope(s) on Cln101 is not known.

Soppet and Dillon teaches polyclonal antibodies generated by the cln101 molecule (referred to by Soppet and Dillon as "SEQ ID NO:2") that specifically bind cln101 in vivo or in vitro (see lines 55-65 of column 19, in particular). Soppet and Dillon further teaches said antibodies as Fab fragments (lines 45-55 of column 19, in particular), conjugated to a growth inhibitor agent or a cytotoxic agent (lines 14-19 of column 20, in particular), in compositions comprising a carrier (lines 1-3 of column 16, in particular), and detectably labeled with a label selected from the group comprising radioisotope, fluorescent, enzymatic, biotin, and gold particle (lines 20-31 of column 20, in particular).

Although Soppet and Dillon do not specifically teach polyclonal antibodies generated by Cln101 protein would internalize or would compete for binding to the same epitope as the epitope bound by antibodies produced by a hybridoma selected from the group consisting of ATCC accession number PTA-5877 and PTA-5876, cln101 antibodies of the claimed kit appear to be the same as those of the prior art, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the cln101 antibodies of the prior art do not possess the same characteristics of the cln101 antibodies of the claimed product. In the absence of evidence to the contrary, the burden is on Applicant to prove that the cln101 antibodies of the claimed product are different from that taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989).

Allowable Subject Matter

Claims 29, 45, 46, and 51 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642